13. The method of claim 12, wherein one or more of the protective antigens is from a pathogen other than *H. somnus*.

Please add the following new claims 14 and 15:

14. The method of claim 1, wherein an immunoglobulin binding site inactivated in the administered organism is encoded by wild type *H. somnus* gene p120.

15. The method of claim 1, wherein the administered organism is administered as a pharmaceutically acceptable vaccine composition.

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons which follow.

A. No New Subject Matter is Presented by the Amendments

After amending the claims as set forth above, claims 1, 5, 6 and 8-15 are now pending in this application.

Claim 1 has been amended to include the limitations of original claims 2,3 and 7, now cancelled. Support for the amendments is found at places throughout the application including, without limitation, original claims 2, 3 and 7. No new subject matter is added by this amendment.

Claims 9-13 have been amended to be singly dependent claims. Withdrawal of the objection to these claims under 37 CFR §1.75(c), and examination of each on the merits, is therefore requested.

The remainder of the amendments made to the claims are grammatical in nature, and are intended to clarify the nature of the invention without expanding the scope of the claims. For example, the term "administered organism" is now used with respect to the *H. somnus* vaccine referenced in the original claims. This change clarifies that the vaccine whose use is claimed comprises *H. somnus* organisms which possess the characteristics defined in claim 1 (see, e.g., Specification at page 4, line 24 through page 5, line 5; vaccine comprises *H. somnus* organisms which express diminished amounts of Ig binding proteins). No new subject matter is added to the claims by these amendments.

Newly added claim 14 specifies that one immunoglobulin binding site inactivated in the administered organism is the site encoded in the virulent organism by *H. somnus* gene p120. Support for this claim is found, for example, in the Specification at page 14, lines 23-33.

Newly added claim 15 specifies that the vaccine used in the invention may be prepared in a pharmaceutically acceptable composition for administration to cattle. Support for this claim is found, for example, in the Specification at page 8, lines 1-16.

Entry of the amendments is respectfully requested.

B. Response to Rejection of Claims 1-5 and 7-8 Under 35 USC §112, First Paragraph

The claims are objected to for lack of enablement, in view of Briggs, *et al.*'s brief observation that *Pasteurellaceae* organisms "have proven difficult to genetically manipulate." Col. 1, Background of the Invention.

The test for enablement of an invention is whether one of ordinary skill in the art would, based on the patent disclosure, have a reasonable expectation of being able to practice the invention. In that respect, the disclosure "must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *In re*

Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The amount of experimentation required for experimentation it to be "undue" is a function of the following factors:

1) the quantity of experimentation necessary;
2) the amount of direction or guidance presented;
3) the presence or absence of working examples;
4) the nature of the invention;
5) the state of the prior art;
6) the relative skill of those in the art;
7) the predictability of the art and
8) the breadth of the claims.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

The Office Action contends that Applicants have not provided working examples of the invention. Yet Applicants *have* provided working examples commensurate with the scope of the claimed invention.

In particular, organisms having the claimed characteristics were selected and purified from natural isolates, and deposited by the inventors with the American Type Culture Collection (strains 1P, 129Pt, 130Pfl and 133P, deposited on September 1, 1999; Specification at p. 3, line 32 through page 4, line 2, and claim 11). Methods for constructing *H. somnus* organisms to be used in the invention from virulent wild-type organisms are detailed at various places throughout the Specification, including in Example 2 (pages 11-15). The particular protocol used by the inventors to inactivate the p120 gene, and alternative protocols, are described in detail at page 14, line 5 through page 15, line 4. Thus, methods for obtaining administered *H. somnus* organisms, as well as actual products of those methods, are well described and exemplified in the Specification.

As claimed, the vaccine compositions for use in the invention shed less endotoxin, and are more susceptible to killing with bovine complement, than virulent wild type *H. somnus*. Both characteristics are associated with loss of immunoglobulin binding protein

expression. Data demonstrating the presence of such characteristics in administered organisms are provided in the Specification, as are methods for inactivating expression of Ig binding proteins. See, e.g., page 5, lines 2-5 (administered organisms on deposit have deletions of the p120 and p76 Ig binding protein genes); page 14, lines 23-33 (inactivation of p120 gene by induced recombination in a wild type *H. somnus* strain); and page 5, lines 22-32 (amount of lipooligosaccharide endotoxin released by a administered *H. somnus* organism whose use is claimed is less than 10% of that released by a virulent strain, such as strain 2336, in Example 1).

Methods for vaccinating cattle with *H. somnus* are well known, and referenced in the Specification (see, e.g., page 3, lines 25-33). One of ordinary skill in the art would expect an *H. somnus* organism, in which only expression of one or more Ig binding proteins is lacking, to be immunogenic in a vaccination protocol. Nothing about the fact that the organism acquired the claimed characteristics naturally or by genetic engineering would alter that expectation.

Briggs, *et al.* is cited for the contrary proposition; i.e., that one of ordinary skill would have difficulty genetically modifying *H. somnus*. However, Briggs, *et al.* itself provides evidence that such a modification was in reach of those of ordinary skill in the art *at least 3 years before the filing date of the present application*, when the Briggs, *et al.* application was filed and reported development of administered *Pasteurellacae* organisms, including *H. somnus*. Indeed, a trivalent vaccine developed by Briggs, *et al.* has since been sold for use in vaccination protocols in cattle, thereby establishing that one of ordinary skill *would* reasonably expect to be able to produce a genetically administered *Pasteurellacae* organism for use in a vaccine. See, "*Scientists Create First Genetically Engineered Vaccine for Shipping Fever,*" from agbuy.com, submitted herewith. Thus, Applicants' disclosure clearly satisifies at least the first and fourth through eighth of the *In re Wands* criteria for enablement.

Moreover, the application provides both working examples of, and specific guidance for, practice of the invention (the first and second of the *In re Wands* factors).

The characteristics desired in an effective *H. somnus* vaccine (susceptibility to complement), the possession of such characteristics by the claimed vaccine preparation, how to make the claimed vaccine preparation, methods for using the claimed vaccine preparation, and models for testing immunity to disease following administration of the claimed vaccine preparation are all described in detail in the application at, respectively: page 4, line 14 to page 5, line 5 (serum-sensitivity of the administered organism); Example 1 (reduction of endotoxin release by the administered organism as compared to wild-type; data also summarized at page 5, lines 22-32); Example 2 (manufacture of vaccine); page 8, lines 1-10 (pharmaceutical preparation of the vaccine); and lines 17-32 (models for confirming the *in vivo* efficacy of the vaccine preparation).

In the latter respect, those of ordinary skill in the art would unquestionably expect the vaccine to be protective. The *H. somnus* bacterin, outer membrane protein extracts, and live cell preparations have been used for vaccination purposes for many years. *See, e.g.,* Potter, *et al.*, at Col. 1, lines 24-42; and Briggs at Col. 1, lines 16-25. Potter, *et al.* teach that you can modify the *H. somnus* organism while retaining a protective level of immunogenicity, even if the modification made resulted in a phenotype not found in nature (an iron regulated protein enriched formulation).

In the vaccine preparations of the current invention, the organism possesses or is administered to have the characteristics of a particular natural isolate of *H. somnus*, found in the prepuce of normal bulls. Specification at page 3, line 26 through page 4, line 13. The deletion of Ig binding protein encoding genes in the natural isolate render it both serum sensitive and less capable of producing endotoxin. Specification at page 4, line 14 through page 5, line 5. Having a natural *H. somnus* phenotype, the organism will necessarily be protective as utilized in the claimed vaccination method.

Based on the foregoing, Applicants respectfully submit that enablement of the amended claims is clearly provided by the present specification. Reconsideration and withdrawal of the rejection of the claims under §112, first paragraph, is therefore requested.

C. Response to Rejection of Claims 1 and 6 Under §102(e)

Potter, *et al.* is cited against Claims 1 and 6 based on its reference to use of a commercial *H. somnus* bacterin preparation to vaccinate cattle. The invention, however, is not directed to use of such a *H. somnus* bacterin. It is instead directed to use of an *H. somnus* organism from which Ig binding protein encoding genes are missing. Potter, *et al.* does not contain any suggestion that an organism possessing this phenotype might exist or be manufactured, and therefore does not anticipate the present claims.

Reconsideration and withdrawal of the claims rejection under §102(e) is respectfully requested.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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MARKED UP VERSION SHOWING CHANGES MADE

Below are the marked up amended claim(s):

1. (Amended) A method for vaccinating cattle against *Haemophilus somnus* [diseases mediated by] infection, comprising administering [an effective amount of] an immunogenic *H. somnus* [vaccine] organism to the cattle, wherein the [*H. somnus*] administered organism possesses characteristics different from those of the wild type virulent organism, the differences comprising the lack of expression of one or more immunoglobulin binding proteins produced by the wild type virulent organism, [is susceptible] susceptibility to killing by bovine complement-containing serum, and reduced shedding of endotoxin during growth.

2. *Cancelled.*

3. *Cancelled.*

4. *Cancelled.*

5. (Amended) The method of [any of] claim[s] 1 [to 4], wherein the administered organism [is] comprises a live vaccine.

6. (Amended) The method of [any of] claim[s] 1 [to 4], wherein the administered organism comprises a [is] killed vaccine.

7. *Cancelled.*

8. (Amended) The method of claim 1 [7], wherein [the lack of expression of] one or more immunoglobulin binding proteins [is achieved] are missing from the administered organism [by the step of genetically engineering *H. somnus* to delete] as a

result of the deletion of one or more genes encoding the one or more immunoglobulin binding proteins from the *H. somnus* genome.

9. (Amended) The method of [any of] claim[s 1 to] 8, wherein the [*H. somnus*] administered organism further expresses [a] one or more protective antigens.

10. (Amended) The method of claim 9, wherein the protective antigen is a 40 kDa *H. somnus* outermembrane protein.

11. (Amended) The method of [any of] claim[s] 1 [to 10], wherein the [*H. somnus*] administered organism is selected from the group consisting of PTA-600, PTA-601, PTA-602 and PTA-603, deposited with the American Type Culture Collection.

12. (Amended) The method of [any of claims 1 to 11] claim 9, wherein the [*H. somnus*] administered organism is genetically engineered to express said one or more protective antigens.

13. (Amended) The method of claim 12, wherein [the *H. somnus* is genetically engineered to express] one or more of the protective antigens is from a pathogen[s] other than *H. somnus.*

(Newly Added) 14. The method of claim 1, wherein an immunoglobulin binding site inactivated in the administered organism is encoded by wild type *H. somnus* gene p120.

(Newly Added) 15. The method of claim 1, wherein the administered organism is administered as a pharmaceutically acceptable vaccine composition.